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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,169	10/21/2003	R. Kent Hermsmeyer	HME/7961.0013	3934

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	**PAPER NUMBER**
1617	
MAIL DATE	**DELIVERY MODE**
08/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,169	HERMSMEYER, R. KENT	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *17-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the receipt of the amendments and remarks received in the office on 5/10/2007, amending claims 1 and 8. Claims 1-16 are currently pending.

Response to Remarks

Applicant's arguments with respect to the rejections of the claims have been considered but are moot in view of the new grounds of rejection. Applicant's amendment necessitated the following rejections. The office Action is made Final.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 8-12, 15, 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hermsmeyer (U.S. 6,056,972) in view of Meyers et al. (J Med Chem, 2001, 44, 4230-4251) and further in view of Weihua et al. (PNAS, 2002, 99, 13589-94).

Hermsmeyer teach a method of reducing coronary artery reactivity and teaches that comprising administering estradiol 17β (via syslastic implants) (serum level, 104 +/- 10 pg/ml) and progesterone (a progestin) reduced the incidence of coronary vasospasm in monkeys (col. 18, Table 3).

The reference does not teach that the potency of estradiol to ER β is higher than that of genistein.

Myers teach from the data that estradiol is more potent towards ER β than genistein (p 4241, Table 4). Meyers et al. teach diarylpropionitrile as an ER-beta potency selective ligand (p 4231, para 2, lines 1-3).

The reference does not teach the 5α-androstane-3β,17 β-diol or any of the derivatives in reducing the incidence or severity of vascular hyperreactivity.

Weihua et al. teaches 5α-androstane-3β,17 β-diol to be an estrogen receptor beta agonist ligand (see Abstract).

Myers teach that estradiol is more potent towards ER β than genistein. The examiner would like to point out that the patent office does not have the facility to determine the potency of compounds in vitro on Ca2+ responses in rhesus coronary ventricular muscle cells. It would have been obvious to one of ordinary skill in the art at the time of invention to administer 5α-androstane-3β,17 β-diol and its derivatives for estradiol 17β in a method for reducing the incidence or severity of vascular hyperreactivity. A person of ordinary skill in the art would have been motivated to do so because by administering one estrogen receptor beta agonist for another one can expect success in regards to the therapeutic treatment of vascular hyperreactivity treatment with similar or superior efficacy of the drug.

It would have been obvious to one of ordinary skill in the art at the time of invention to administer diarylpropionitrile (DPN) for estradiol 17β. The motivation to do so is provided by Myers et al. Minshall teaches that vascular hyperreactivity and the ability to provoke coronary vasospasm can be normalized by adding physiological levels of estradiol and Myers teach the DPN has more potency towards ER β ligand. Hence

by administering DPN, an estrogen receptor beta agonist that is more potent than estradiol a person of ordinary skill in the art would have been motivated by the expectation of success and in achieving at least similar or superior therapeutic benefits in the treatment of vascular hyperreactivity compared to estradiol.

The compounds in claims 5 and 6 are derivatives of 5α-androstane-3β,17 β-diol and are rejected based on close structural similarity to 5α-androstane-3β,17 β-diol. It is obvious that compounds with very close structural similarities will have similar utilities and hence the derivatives of 5α-androstane-3β,17 β-diol will function as estrogen beta-receptor agonists.

The examiner would like to point out that a prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (discussed in more detail below) and In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991).

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hermsmeyer (U.S. 6,056,972) in view of Meyers et al. (J Med Chem, 2001, 44, 4230-4251) and further in view of Weihua et al. (PNAS, 2002, 99, 13589-94) as applied to claims 1, 2, 4-6, 8 above and further in view of Barkheim et al. (Molecular Pharmacology, 54, 105-112, 1998).

The teachings of Hermsmeyer, Meyers et al. and Weihua et al have been discussed in the 103(a) rejection set forth above.

The references do not teach epiestriol in reducing the incidence or severity of vascular hyperreactivity.

Barkheim et al. teaches that epiestriol has an ER-beta selective agonist potency.

It would have been obvious to one of ordinary skill in the art at the time of invention to administer epiestriol for estradiol 17 β in a method for reducing the incidence or severity of vascular hyperreactivity. The motivation to do so is by administering one estrogen receptor beta agonist for another would provide similar or superior efficacy in the therapeutic treatment of vascular hyperreactivity.

Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hermsmeyer (U.S. 6,056,972) in view of Meyers et al. (J Med Chem, 2001, 44, 4230-4251) and further in view of Weihua et al. (PNAS, 2002, 99, 13589-94) as applied to claims 1, 2, 4-6, 8 above and further in view of Burry et al. (J of Obstet Gynecol, Jun 1999, 1504 – 1511).

The teachings of Hermsmeyer, Meyers et al. and Weihua et al have been discussed in the 103(a) rejection set forth above.

The references do not teach the topical application of estradiol 17 β in a method for reducing the incidence or severity of vascular hyperreactivity.

Burry et al. teach transdermal application of estradiol in postmenopausal women (see Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer estradiol 17 β topically because Burry et al. teach transdermal application of estradiol in postmenopausal women. A person of ordinary skill in the art would have been motivated to administer estradiol topically because of expectation of success and Burry had already shown the safety of the drug and it can applied transdermally.

Response to Arguments

Applicant's arguments with respect to the rejections of the claims have been considered but are moot in view of the new grounds of rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER